FDA Proposes Rules to Guard Against Spread of 'Mad Cow' Disease

FDA, From A1

prevent it from becoming one. Those included increased monitoring for Creutzfeldt-Jakob disease and a review of livestock practices, which led to the new proposal.

The FDA estimates that the new rule will cost between $21 million and $48 million a year, with most of the burden borne by the rendering industries. Soy-based feeds will likely have to be supplemented to provide all of the nutrients in meat-based products. Kessler said that those price increases would probably not be felt by consumers.

Bruce Blanton, executive director of the National Renderers Association in Alexandria, said that he had not had time to digest the proposal and was reluctant to comment on its specifics. In general, however, "the science there is unclear," Blanton said. "It's not crystallized black and white." As for the agency's estimate of the cost to industry, Blanton said, "just on the first blush of it, it seems way too low." When the FDA first announced in May that was looking into proposing a rule, the renderers filed a comment with the agency opposing bans on such "ruminant-to-ruminant" feeds.

The beef industry supported the agency move. "We applaud the federal government for its continued efforts to prevent BSE from occurring in the U.S. cattle herd," the National Cattlemen's Beef Association said in a statement. The organization noted that beef and dairy producers voluntarily removed "ruminant-derived" proteins from their feed last April, and had used relatively little of the available by-products before that time.

Consumer advocates hailed the changes as well. A representative of a consumer group that had called for a broad animal-derived feeds ban praised the proposal yesterday. Robert Hahn, director of legal affairs and research for the the advocacy group Public Voice for Food and Health Policy, said that the new rules "sound like what we wanted," but warned, "This is only a proposal, and there may be a big fight ahead. . . . The U.S. should not be complacent about this problem," Hahn said.

"If they get it implemented it will do a great job" in preventing the spread of BSE, said Richard F. Marsh of the University of Wisconsin at Madison. Marsh, one of the leading heralds of the risks of the disease in this country, called the FDA proposal "a really significant step."

Kessler said that the agency considered more and less stringent animal feed rules. Regulators rejected banning the use of animal-derived feeds for all mammals, for example, because transmission of the diseases has not been seen in animals such as pigs. For the same reasons, the proposal also does not apply to chicken feed.

A less restrictive version of the rule that would have merely restricted the use of feeds made from the body tissues most likely to carry the "prions" linked to the diseases (chiefly, the brain and spinal cord) was rejected as unworkable in practice, Kessler said.

Elk and mink will also be excluded from ruminant feeds under the FDA proposal. Bovine blood, and milk and gelatin from ruminants will be allowed in feeds, since those substances do not carry the agents of the diseases, known collectively as "transmissible spongiform encephalopathies."

The British government has also taken steps to head off the spread of the disease. Changes in rendering practices beginning in 1989 were instituted to block the ability of the disease from spreading via animal feeds, and thousands of sick cows were destroyed to prevent any transfer to humans via the food supply. The first case of BSE was reported in the United Kingdom in 1986.

The FDA proposals will now undergo a 45-day comment period, after which the agency will analyze the comments and issue a final rule, probably within months.

FDA Moves On 'Mad Cow' Disease Rules

Proposal Targets Use Of Carcasses in Feed

By John Schwartz
Washington Post Staff Writer

The Food and Drug Administration yesterday proposed tough new rules to protect Americans from "mad cow" disease.

The proposal would ban the practice of feeding cows, sheep and goats mixtures containing ground up carcasses of animals that could be infected with the disease.

While no cases of "mad cow" disease have been reported in this country, the incubation period is several years. The new rules, then, are designed to keep any disease that might have reached this country from spreading rapidly through feed products.

"If there were a case [of the disease] to be found in this country—and there is no case that we know of—the steps that we're taking would confine the spread and reduce whatever risk there is to humans even further," said FDA Commissioner David A. Kessler, who called the new rules a "fire wall."

Last year, the British government announced that there appeared to be a link between "mad cow" disease, also known as bovine spongiform encephalopathy or BSE, and 10 cases of a new variant of the Creutzfeldt-Jakob disease, a rare but devastating human disease that progressively and fatally destroys brain tissue.

The announcement caused widespread panic among British consumers, and prompted a ban on British beef in Europe. Subsequent studies have supported the theory that the humans got the disease from eating contaminated beef. The beef contamination is believed to have occurred because the animals were given feed manufactured from the carcasses of sheep infected with a similar disease, scrapie.

U.S. health officials assured the public that the disease was not a threat in this country, but took several steps to

See FDA, A21, Col. 1

BIOWORLD® TODAY
THE DAILY BIOTECHNOLOGY NEWSPAPER
FRIDAY
DEC. 20, 1996
VOLUME 7, NO. 247
PAGE 1 OF 4

Cell Genesys To Get $26M In Gene Activation Pact With Hoechst

By Charles Craig
Staff Writer

Hoechst Marion Roussel agreed to pay Cell Genesys Inc. up to $26 million for its gene activation technology to produce two protein drugs, one of which is erythropoietin, a red blood cell booster used to treat anemia.

The deal represents Hoechst Marion Roussel's second license for technology to help it enter the lucrative market for therapeutic proteins, particularly erythropoietin, or EPO. Transkaryotic Therapies Inc., of Cambridge, Mass., owns the other gene activated protein production technique licensed by Hoechst Marion Roussel, of Frankfurt, Germany.

Both gene activated technologies involve stimulating production of therapeutic proteins in human cells, which

See Cell Genesys, Page 3

Lacking DNA, RNA, Prions Transmit Disease By Refolding 3-D Structure

By David N. Leff
Science Editor

A pathogenic particle 100 times smaller than the smallest virus, could conceivably bring down the government of British Prime Minister John Major.

This week, Major added another 100,000 head to the 1.2 million cattle that Britain is slaughtering, to check the epizootic of "mad cow disease," which has plagued the country for the past decade. His latest hike in the number of animals marked for destruction has the aim of reversing a ban on British beef exports imposed last March by the European Union.

That embargo was in reaction to fear of possible contagion affecting the human form of the fatal bovine transmissible spongiform encephalopathy that has decimated British herds. That human equivalent is an equally deadly brain infection, Creutzfeldt-Jakob Disease (CJD).

See Prion, Page 4

Preclinical Problems Surface With A Second Cortech Drug

By Charles Craig
Staff Writer

A Phase II pilot study of Cortech Inc.'s CE-1037, a parenteral elastase inhibitor, for acute respiratory distress syndrome has been suspended after partner Hoechst Marion Roussel said safety concerns with the drug surfaced in recent animal studies.

Joseph Turner, chief financial officer with Denver-based Cortech, said Hoechst Marion Roussel, of Frankfurt, Germany, also has ended their collaboration on CE-1037, returning all rights to the product.

Turner did not know details of the preclinical studies Thursday. Frankfurt-based Hoechst AG, parent of Hoechst Marion Roussel, took over development of CE-1037 in 1995 when the German drug maker acquired Marion Merrell Dow, of Kansas City, Mo.

No adverse events have occurred in any clinical trials with CE-1037, Turner added. Patients were being enrolled in

See Cortech, Page 2

Amylin Pharmaceuticals Begins Pivotal Phase III Diabetes Trials

By Lisa Seachrist
Washington Editor

Amylin Pharmaceuticals Inc. has initiated four additional pivotal clinical trials of its diabetes therapy pramlintide. These U.S. and European Phase III trials complement two other Phase III trials begun in 1995 to test whether pramlintide offers additional blood glucose control to diabetics on insulin and thereby reduces the risk of complications like blindness, kidney failure and nerve damage.

The trials are randomized, double-blind, placebo-controlled experiments that will involve a total of 2,600 patients at more than 200 sites in the U.S., Europe and Canada and will test the product in patients with both type I diabetes and type II diabetes that require insulin. The San Diego, company intends to submit pramlintide for approval in North America and Europe by the end of 1998 assuming patient enrollment proceeds as planned.

"Pramlintide could be an important adjunctive therapy

See Amylin, Page 2

OTHER NEWS TO NOTE

• **Ligand Pharmaceuticals Inc.** of San Diego, said that Targretin, the company's lead retinoid-based therapeutic compound, has demonstrated efficacy as a chemopreventive agent in a well studied, pre-clinical animal model of breast cancer — the NMU-induced rat mammary carcinoma model. Targretin-treated animals in the study showed a 90 percent reduction in tumor burden and tumor incidence compared to controls. The study results also indicated that Targretin may offer significant reductions in side effects over other breast cancer chemotherapy agents.

• **NeXstar Pharmaceuticals Inc.,** of Boulder, Colo., said that research published in the *Journal of Clinical Investigation* provides the first demonstration of *in vivo* efficacy of an aptamer directed against a cell surface receptor. In the paper, scientists from NeXstar and their collaborators describe a series of aptamers, generated by the company's proprietary SELEX combinatorial chemistry process that bind specifically and tightly to L-selectin, a cell surface receptor found on the surface of most leukocytes.

• **Quintiles Transnational Corp.,** of Research Triangle Park, N.C., has been added to NASDAQ-100 Index of the largest and most active non-financial issues listed on the NASDAQ Stock Market. Quintiles' total market value of approximately $2 billion is four times greater than the $500 million minimum for listing on the index.

Amylin

Continued from Page 1

for the 7 million diabetics that rely on insulin," said Richard Krawiec, director of corporate communications for Amylin.

Pramlintide is an analog of the hormone amylin which is produced by the same pancreatic cells that supply the body with insulin. In 1987, researchers discovered that amylin may play an important role in blood glucose regulation. Specifically, amylin appears to control the rate at which food enters the intestines and the bloodstream. Diabetics typically lack adequate amounts of the hormone, and as a result, they have huge amounts of glucose pouring into their bloodstreams after meals instead of getting a steady release of glucose.

"Amylin serves to regulate the amount of glucose that makes it into the bloodstream whereas insulin removes sugar from the bloodstream," said Krawiec. "With both mechanisms disabled, diabetics have very poor control over the amount of glucose in their bloodstreams. And, glucose is the toxic molecule that causes the complications of diabetes."

Scientists at Amylin pharmaceuticals modified the hormone to make it less sticky and easier to inject. Phase II trials of pramlintide showed that diabetics using the drug in addition to their insulin regimen had statistically significant improvement in glucose control. Amylin and their clinical collaborators, Johnson & Johnson, now are testing whether the drug improves glucose control in the long term. They are also testing to see if they can reduce the dosing schedule from four shots per day.

"It's been 75 years since the discovery of insulin and that has been a life saver," Krawiec said. "But, insulin doesn't give adequate glucose control. Pramlintide may offer diabetics on insulin that control." ■

Cortech

Continued from Page 1

the Phase II trial for acute respiratory distress syndrome when it was suspended. A review of the preclinical safety data will be conducted before deciding how to proceed.

Another Phase II trial of the elastase inhibitor for cystic fibrosis has been completed and results are being analyzed.

Turner said Cortech received $1 million in 1996 from Hoechst in support of the CE-1037 program.

Two months ago SmithKline Beecham plc, of London, suspended a Phase II trial of Cortech's Bradycor after safety concerns were raised in rat studies being conducted for the pharmaceutical firm by an outside contract research organization.

As with CE-1037, Bradycor, a bradykinin inhibitor, was not associated with any adverse reactions among patients in any clinical trial. The Phase II study of Bradycor for prevention of brain damage from head injuries was nearly completed when it was stopped.

Turner said the trial, which had enrolled 130 of 160 patients, will not be resumed. Bradycor's performance will be evaluated based on the data already collected and results are expected in the first quarter of 1997.

The preclinical safety problems with Bradycor remain unexplained, he added.

Cortech's stock (NASDAQ:CRTQ) closed Thursday down $0.188 to $1.437. ■

BIOWORLD® TODAY is published every business day by the BioWorld® Publishing Group, a division of American Health Consultants®, 3525 Piedmont Road, Building Six, Suite 400, Atlanta, GA 30305. Opinions expressed are not necessarily those of this publication. Mention of products or services does not constitute endorsement. BIOWORLD® and BIOWORLD® TODAY are trademarks of American Health Consultants®, a Medical Economics Company.

ATLANTA NEWSROOM: Senior Managing Editor: **Lynn Yoffee.** Staff Writers: **Charles Craig, Frances Bishopp.** Production Editor: **Amy Wesolowski.**
EAST COAST BUREAU: Science Editor: **David N. Leff.** Washington Editor: **Lisa Seachrist.**
WEST COAST BUREAU: Business Editor: **Jennifer Van Brunt.**
CORPORATE OFFICE: Publisher: **Donald R. Johnston.** Marketing Manager: **Paige Stanfield.** Operations Manager: **Daren Wang.** Account Representatives: **Ron Morgan, Karen Wehye.**

SUBSCRIBER INFORMATION
Please call (800) 879-8790 to subscribe or if you have fax transmission problems. Outside U.S. and Canada, call (404) 262-5526. Our customer service hours are 8:30 a.m. to 6:00 p.m. EST.

EDITORIAL
Lynn Yoffee. (404) 262-5454
Charles Craig. (404) 262-5423
Frances Bishopp. (404) 262-5413
Fax: (404) 814-0759
Lisa Seachrist. (202) 289-4798

Publisher: Donald R. Johnston
(404) 262-5439

Internet: http://www.ahcpub.com

Cell Genesys

Continued from Page 1

otherwise would not produce them, as a means of avoiding intellectual property restrictions on marketing the drugs.

Therapeutic proteins, such as EPO, insulin and growth hormone, currently are made by patented recombinant technologies involving introduction of cloned human genes in non-human cells.

Hoechst Marion Roussel's alliances with Cell Genesys, of Foster City, Calif., and Transkaryotic Therapies license their technologies specifically for EPO.

If successful in getting to market with the red blood cell booster, Hoechst Marion Roussel would compete with Amgen Inc., of Thousand Oaks, Calif., which developed the recombinant version, and its partner, Johnson & Johnson, of New Brunswick, N.J.

However, some Wall Street analysts have suggested the battle's initial front will be the courthouse with litigation over patent rights.

In its deal with Cell Genesys, Hoechst Marion Roussel, a subsidiary of Frankfurt-based Hoechst AG, paid $4 million up front and will contribute another $22 million in milestone payments.

Hoechst Marion Roussel is expected to enter clinical trials in 1997 with a Transkaryotic Therapies gene activated EPO drug. Plans for development of a Cell Genesys gene activated EPO drug were not disclosed. Hoechst Marion Roussel officials also would not discuss differences or similarities in the Transkaryotic Therapies and Cell Genesys technologies.

The pharmaceutical company's deals with Cell Genesys and Transkaryotic involve a second protein, but in each instance it has not been identified.

The alliance with Hoechst Marion Roussel is Cell Genesys' second. The two companies are collaborating on an AIDS gene therapy that could be worth up to $160 million to Cell Genesys. The deal included an equity investment, giving Hoechst a 13 percent stake in Cell Genesys.

Cell Genesys' chief financial officer, Kathleen Glaub, said her company has received $45 million from Hoechst since the AIDS program began in October 1995. The gene therapy involves genetically modifying killer T cells to destroy HIV-infected immune system cells.

In Cell Genesys' gene activation technology, regulatory DNA elements are inserted into chromosomes to turn-on the gene responsible for expressing the specific protein of interest.

Akzo Nobel Pharma Group, of Arnhem, the Netherlands, was the first company to collaborate with Cell Genesys on a gene activation product. In 1994, the two signed an agreement for development of follicle-stimulating hormone (FSH) for treatment of infertility.

In addition to releasing news of the Hoechst deal, Glaub also said Thursday Akzo paid Cell Genesys $5 million to end that alliance and return rights to gene activated FSH.

Akzo had developed a recombinant version of FSH and it began selling that product recently following settlement of a patent fight with Ares-Serono, of Geneva.

Akzo retains a non-exclusive license to Cell Genesys' gene activation technology.

Cell Genesys' stock (NASDAQ:CEGE) closed Thursday up $0.875 to $8.37. ■

OTHER NEWS TO NOTE

• **Shaman Pharmaceuticals Inc.,** of South San Francisco, said that Ono Pharmaceutical Co., Ltd., of Japan, has paid Shaman, $1 million for enhanced rights to develop and commercialize Shaman's diabetes compounds.

Clarification

A headline on an article about a Genelabs Technologies Inc. collaboration in the Dec. 19, 1996 *BioWorld Today* should have clarified that the agreement was made with Dupont Merck Pharmaceutical Co.

Prion

Continued from Page 1

Major lost his majority in Parliament last week, leaving his government's survival at the mercy of votes by Northern Ireland's Ulster Unionist Party. As *The New York Times* pointed out on Dec. 17, Northern Ireland "has the most grass-fed herds, and has suffered the fewest cases of the [mad cow] disease."

What both the bovine and human afflictions have in common is an enigmatic, submicroscopic pathogen called the "prion" — "proteinaceous infective agent." (See *BioWorld Today*, April 8, 1996, p. 1.)

Besides cows, the prion infects sheep and goats with scrapie, and mink with encephalopathy. In humans, besides CJD, it causes fatal familial insomnia (FFI), as well as Gerstmann-Strassler-Scheinker syndrome. (See *BioWorld Today*, Aug. 10, 1995, p. 1.) These are all extremely rare diseases; incidence of CJD runs one in a million cases, ten percent of them familial. FFI, with perhaps 20 to 50 known victims in the world, is infinitely more exotic.

When neurologist Stanley Prusiner propounded his discovery of the prion in 1981, he described it as a protein devoid of nucleic acid, and totally unlike any virus, viroid, fungus or bacterium known. The doubts (not to mention hoots and scoffs) his claim raised at the time have largely dissipated. Prions now have recognition as causing diseases in man and beast, and these are widely researched today.

Three Prion Transmissibility Persuasions

It seems that, unique among diseases, the prion-inflicted ones are both inherited, infectious and spontaneous versions.

Neurophysiologist Stephen DeArmond, a co-author of the *Science* paper, told *BioWorld Today*: "Mutations in the prion protein gene destabilize the molecule, and causes it spontaneously to form pathogenic prion protein particles.

"The other form," DeArmond continued, "are those forms of prion disease actually acquired by infection, of which we believe the variant CJD in Great Britain is one example. But 90 percent of the cases do not seem to be caused by a genetic predisposition, that is, a mutation, nor by an infection. We call that sporadic CJD, caused by a spontaneous thermodynamic conversion from the normal to the abnormal structural form of the protein."

What remains is the large question: How can a pathogen containing no nucleic acid whatsoever transmit diseases, from cow to cow, and presumably person to person?

Prusiner, at the University of California, San Francisco, holds that a change in 3-D protein structure rather than a gene transformation, is the answer, and has enlisted transgenic mice to tackle this conundrum. His paper in today's *Science* bears the title: "Evidence for the conformation of the pathologic isoform of the prion protein enciphering and propagating prion diversity."

Prusiner points to the fact that 3-D normal prion protein "has a high α-helical content and is virtually devoid of β-sheets, whereas [mutant prion protein] has a high β-sheet content." This profound conformational change, he observes, which converts the benign to the pathogenic, "is a post-translational process that does not appear to involve a covalent modification of the protein."

These structural β-sheets," Prusiner has pointed out, have a possible bearing on Alzheimer's disease. All amyloids studied to date," he told *BioWorld Today* two years ago, "have a β-pleated sheet structure." (See *BioWorld Today*, Feb. 10, 1994, p. 1.)

The transgenic chimeric mice his laboratory has constructed carry a combined murine and human prion gene, which renders them susceptible to human prions. The co-authors injected extracts from patients dead of either CJD or FFI into the animals' brains.

The mutant prion proteins that cause these disorders are chemically similar, but differ in their 3-D structure. When Prusiner's co-authors cleaved CJD material with an enzyme *in vitro*, they got a 21-kiloDalton fragment. FFI brain extracts came up 19 kiloDaltons.

So they asked their mice whether the human prions put into their living brains inherit the same differing CJD and FFI fragments. The answer: They did. About 200 days after inoculation, FFI material produced the 19 kD mutant human brain fragment. Extracts from both familial and sporadic CJD brains yielded the 21 kD version.

"This result," the *Science* paper concluded, "suggest[s] a mechanism to explain strains of prions where diversity is encrypted in the conformation of [the mutant prion protein].

Viral Nucleic Acid Adherence

But neurologist Michael Harrington at California Institute of Technology, in Pasadena, and many others in the field, persist in suspecting that somewhere in the prion haystack lurks a virus that transmits the diseases. As quoted in an editorial titled "Ironing out the wrinkles in the prion strain problem," Harrington told *Science* readers: "[Prusiner's] paper is evidence that the conformational differences yield strains," but added that it doesn't prove it."

DeArmond said: "The people who support the viral, or nucleic-acid hypothesis, have no data at all. It's all based on a hope and faith that it's gotta be a virus. Whereas the prion-only hypothesis is based on a mountain of neurochemical data, which shows that the purified agent is the prion protein. If you eliminate the prion protein from an animal, by making knockout mice, you cannot propagate prions or infectivity."

In the editorial, the paper's first author, post-doctoral fellow Glenn Telling, observed: "There are people who will go to their graves believing that these diseases are caused by viruses."

To which Prusiner added: "They can think what they want. I can't help them." ■

Mad cow disease diagnosed in humans

News that mad cow disease might have cropped up in 12 people this spring—perhaps as a result of eating meat from infected British cattle (SN: 4/13/96, p. 228)—sent researchers scrambling to their labs. There they focused on PrP, a protein suspected of causing that disease and some other fatal brain disorders in humans, including Creutzfeldt-Jakob disease (CJD).

Now, British researchers report they have direct evidence that mad cow disease, or bovine spongiform encephalopathy, was indeed transmitted from cattle to people. The evidence lies in PrP's shape, which appears to determine whether it coexists harmlessly with other proteins in brain cells or wreaks havoc.

Earlier studies indicated that normal PrP and its warped, disease-causing alter ego, known as a prion, are biochemically identical. This finding led researchers to conclude that changes in PrP structure result in functional differences, which would account for the different symptoms among infected species. They also theorized that a prion, which has no genetic material, replicates by twisting normal PrP into its own image.

John Collinge of the Prion Disease Group in the Imperial College School of Medicine at St. Mary's in London and his colleagues report in the Oct. 24 NATURE that they can exploit the different shapes to trace the transmission of prion strains within and between species.

The team used a standard laboratory technique to generate a band pattern for each protein. They found that most prions taken from different hosts formed distinctly different patterns. Since the proteins are biochemically alike, the variations probably signal differences in their shape.

The band pattern of prions taken from people who died of the human variant of mad cow disease matched the pattern from mice and monkeys infected in the lab with mad cow disease. It differed from the band pattern of prions from people with CJD. Such differences could form the basis of a new diagnostic test (SN: 10/12/96, p. 238), the researchers say.

Adriano Aguzzi and Charles Weissmann of Zurich University say in an accompanying editorial that the new work represents "an exciting new approach" to the study of prions and the role they play in these rare brain diseases.

Did rabies fell Edgar Allan Poe?

When literary figure Edgar Allan Poe collapsed in front of Ryan's Saloon in Baltimore on Oct. 3, 1849, everyone assumed the writer's boozy lifestyle had finally taken its toll.

Not so, says R. Michael Benitez of the University of Maryland Medical Center in Baltimore. Benitez' analysis of historical records shows that Poe probably died of rabies, a viral disease of the central nervous system.

Poe was taken to a hospital in Baltimore, where he suffered from delirium and tremors, both common in alcoholics who have not had a drink for 5 to 10 hours. After 3 days, he recovered briefly, then lapsed into delirium and confusion. The writer remained in this state until his death on Oct. 7, 1849.

The relapsing nature of Poe's illness doesn't match the symptoms of alcohol withdrawal, Benitez says. Furthermore, historical evidence suggests that Poe had abstained from alcohol for the 6 months prior to his collapse. He refused an alcoholic drink in the hospital.

The symptoms of Poe's illness mirror those of a rabies infection, Benitez notes in the September MARYLAND MEDICAL JOURNAL. Even more telling, Poe had great difficulty drinking water during his hospital stay. Rabies produces involuntary spasms of the throat that make swallowing difficult.

Poe was a well-known animal lover and was especially fond of cats, which can transmit the rabies virus. There was no record of an animal bite preceding Poe's ailment, but the illness can take more than a year to surface, Benitez says.

Iron pills improve kids' test scores . . .

Using dietary supplements to treat iron deficiency improves a girl's learning and memory, a new study finds.

Teenage girls face a particular risk of iron deficiency. "A lot of iron is used up laying down new muscle and expanding the blood volume" to meet the needs of a growing body, explains pediatrician Ann B. Bruner of Johns Hopkins Children's Center in Baltimore. However, this is also the time that girls begin to menstruate. "And it's probably the addition of this [iron loss in] menstrual blood," she says, "that leaves many girls in a negative iron balance during much of puberty."

Working with four local schools—two public, two private—Bruner's team recruited 716 girls age 14 to 18 for blood tests. Of the 112 girls who were iron-deficient but not anemic, 81 entered the study. After giving each girl four tests of attention and memory, Bruner's group randomly assigned half of the teens to receive daily pills containing 260 milligrams of iron and the other half to get identical pills containing no iron. Eight weeks later, all of the girls took the battery of tests again.

"Adults and teenagers with iron deficiency frequently report they have trouble concentrating," Bruner notes. In this study, however, iron had no effect on scores from the three tests measuring attention. It made a difference only on the Hopkins Verbal Learning Test. Here, each girl listened to 12 words and then tried to recall them. The researchers administered the exercise three times, using the same list, and added the correctly recalled words from all three trials.

Both groups of girls scored the same on the initial group of tests. Eight weeks later, the iron-supplemented girls remembered an average of one word more on each of the second and third trials, she reports in the Oct. 12 LANCET. The girls who received the ironfree pills scored the same on both batteries of tests.

Bruner would prefer that teens—especially the 15 percent of girls with iron deficiency—eat an extra serving of perhaps spinach, raisins, or wheat germ three times a week. But as a mother, she's learned that children don't always cooperate, making vitamin and mineral supplements a useful fallback. Indeed, she finds that none of the teenage girls she treats eats breakfast. "They're too busy doing their hair," she says. Then they skip those "nasty" school lunches, snack on chips and sodas after school, and pick up dinner at the fast-food franchise where they work. "Unfortunately," she laments, "this is real."

. . . as does breakfasting near test time

Children who eat breakfast at school score better on tests of verbal learning and memory than kids who either skip breakfast or eat at home, an Israeli study found. Its authors suggest that a meal's effect on learning may trace to how long it elevates concentrations of sugar in the blood.

Pediatrician Nachum Vaisman of Kaplan Hospital in Rehovot and his coworkers studied 569 children age 11 to 13. After giving the children a series of tests, the researchers assigned two-thirds of them to a breakfast of sugared cornflakes and milk at school for the next 2 weeks. At the end of the study, they retested the children, administering the tests just 30 minutes after the school-fed children had completed their meals.

On each of 10 different measures of memory and learning, children who ate at school performed better than those who had eaten at home and at least as well as—but usually better than—those who had skipped breakfast. Vaisman's team suspects that a transient increase in blood sugar explains why the children fed at school outperformed those who had eaten 2 hours earlier at home. They report their findings in the October ARCHIVES OF PEDIATRICS AND ADOLESCENT MEDICINE.